REMARKS

Upon entry of this amendment, claims 5, 9, 12-14, 39, 42, and 50-61 are pending in the instant application. Applicants reserve the right to prosecute the cancelled and deleted subject matter, as well as the originally presented claims, in continuing applications. Claims 5, 9, 51-53, 55 and 57-59 have been amended, and claims 60-61 have been added. The present amendments are fully supported by the specification and the claims as originally filed. Accordingly, no new matter has been added.

Claim Rejections Under 35 U.S.C. § 101

The Examiner has maintained the rejection of claims 5, 9, 12-14, 39, 42 and 50-59 under 35 U.S.C. § 101 for lack of utility. According to the Examiner, the claimed nucleic acids are "not supported by either a specific asserted utility or a well established utility because the specification fails to assert any utility for the claimed nucleic acids or the encoded proteins and neither the specification as filed nor any art of record disclose or suggest any activity for the claimed nucleic acids or the encoded proteins such that another non-asserted utility would be well established." (Office Action, page 2).

Applicants traverse this rejection as the specification provides a specific assertion of the utility for the claimed nucleic acids. The pending claims, as amended herein, are directed to isolated nucleic acids encoding the polypeptide of SEQ ID NO:14 (or a mature form thereof), isolated nucleic acids comprising SEQ ID NO:13 (or the complement thereof) and specific variants of these nucleic acids.

The as-filed specification discloses that these claimed nucleic acids are useful in differentiating certain cancer tissues from the corresponding normal (*i.e.*, non-cancerous) tissues, *e.g.*, in diagnostic tests. For example, the specification discloses that the claimed nucleic acids are present at elevated levels in certain types of prostate cancer (*see e.g.*, Table 12DD on page 223, columns 4-6, line 13) and certain types of lung cancer (*see e.g.*, Table 12DE on page 224, columns 1-3, lines 15-22), including at least one strain of small cell lung cancer (*see e.g.*, Table 12DF on page 226, columns 1-3, line 2). Thus, the nucleic acids of the claimed invention are useful as cancer markers by detecting the level of expression of these specific nucleic acids in a biological sample, *e.g.*, in a tissue sample from a tumor or suspected tumor, and comparing the

expression level with the level in the corresponding normal tissue. Thus, the utility of the claimed nucleic acid molecules is specific, rather than "generally applicable to broad classes" of nucleic acids.

The skilled artisan would appreciate that measurement of the relative amount of nucleic acid in tumor tissue as compared to normal adjacent tissue, *e.g.*, by using the method provided in Example 2 or by another well established method, is useful as a real-world tool in cancer diagnosis. Such expression tests are currently commercially available in the U.S., thereby demonstrating a substantial and credible "real world" utility for an invention of this type.

The Examiner has stated that the asserted utility provided by the as-filed specification is not substantial, because there is no evidence as to "how the ovarian cancer tissue, lung and gastric cancer tissue would be [differentiated]". (Office Action, page 4). However, the claimed nucleic acid molecules are useful in differentiating cancer tissue from its corresponding normal tissue. Thus, the ability to differentiate between cancer types is irrelevant to the asserted utility of the claimed nucleic acid molecules.

Moreover, Applicants submit that those skilled in the art will appreciate that certain genes are differentially expressed in a variety of different cancers. Consistent misexpression of a gene in different cancer types increases that gene's value as a diagnostic tool. First, consistent misexpression raises confidence in the robustness of the marker, and second, consistent misexpression allows one to use a single test in the diagnosis of a variety of cancers. Thus, the fact that the claimed nucleic acids are expressed in several cancer types does not in any way diminish the presence of a "real world" utility for these nucleic acids in a diagnostic test.

Applicants submit, therefore, that the as-filed specification provides a specific, substantial and credible utility for the claimed nucleic acids as markers for cancer, *e.g.*, in diagnostic tests. Accordingly, the claim rejections under 35 U.S.C. § 101 should be withdrawn.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 5, 9, 12-14, 39, 42 and 50-59 under 35 U.S.C. § 112, first paragraph. According to the Examiner, one skilled in the art would not know how to use the claimed invention because it is not supported by either a specific or substantial asserted utility or a well established utility.

Applicants traverse. For the reasons given above, the claimed nucleic acids are supported by a specific, substantial and credible utility in the area of cancer diagnostics. Accordingly, this rejection should be withdrawn.

Claims 5, 9, 51-53 and 57-59 have also been rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had at the time the application was filed. According to the Examiner, "it is unclear what activity the claimed variants possess, what activity the claimed encoded proteins possess and therefore unclear how a person having skill in the art would have used the claimed variants." (Office Action, page 5).

Solely to expedite prosecution of the instant application, the pending claims have been amended herein. In particular, claim 5 has been amended to recite an isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence selected from the group consisting of a mature form of the amino acid sequence SEQ ID NO:14 and SEQ ID NO:14.

Amended claim 9 is directed to an isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:13; and the complement of SEQ ID NO:13.

Claims 51-53 depend from amended claim 5 and recite specific variants of a nucleic acid encoding the amino acid sequence of SEQ ID NO:14, or a mature form thereof. In particular, claim 51 recites a nucleic acid variant, wherein the amino acid residue at position 28 of SEQ ID NO: 14 is Asp or Gly. Claim 52 is directed to a nucleic acid variant, wherein the amino acid residue at position 64 of SEQ ID NO: 14 is Val or Ala. Claim 53 recites a nucleic acid variant, wherein the amino acid residue at position 76 of SEQ ID NO: 14 is Ala or Thr.

Amended claims 57-59, which depend from amended claim 9, recite specific variants of the nucleic acid sequence of SEQ ID NO:13 or the complement thereof. In particular, claim 57 is directed to a nucleic acid variant, wherein the nucleotide residue at position 117 of SEQ ID NO: 13 is A or G. Claim 58 recites a nucleic acid variant, wherein the nucleotide residue at position 225 of SEQ ID NO: 13 is T or C. Claim 59 is directed to a nucleic acid variant, wherein the nucleotide residue at position 260 of SEQ ID NO: 13 is G or A.

The nucleic acids and nucleic acid variants recited by amended claims 5, 9, 51-53 and 57-59 are described throughout the specification as originally filed. For example, the nucleic acids

of amended claims 5 and 9 are disclosed at page 4, lines-21-32 21; at pages 48-67; at page 127, lines 7-27; and at page 129, lines 4-23. The variants recited by amended claims 51-53 and 57-59 are disclosed, *e.g.*, on page 294 of the as-filed specification.

Accordingly, Applicants submit that the amended claims are described by the as-filed specification in such a manner as to allow a person skilled in the art to conclude that Applicants had possession of the claimed invention at the time of filing. Applicants, therefore, request that the Examiner withdraw this rejection.

Claim Rejections Under 35 U.S.C.§ 102

Claim 5 and dependent claims 12-14, 39, 42, 50-53 have been rejected under 35 U.S.C. § 102(b) as being anticipated by International Publication WO 98/02541 by Schaefer *et al.* ("Schaeffer"). According to the Examiner, Schaefer describes polynucleotides encoding polypeptides that comprise residues 1-400 or 450-520 of SEQ ID NO:14, as well as variants where the amino acid residue at position 28 of SEQ ID NO:14 is Asp, where the amino acid residue at position 64 of SEQ ID NO:14 is Val, and where the amino acid at position 76 of SEQ ID NO:14 is Ala.

Claim 5 and dependent claims 10, 12-14, 39, 42, 50-53 have also been rejected under 35 U.S.C. § 102(b) as being anticipated by Oohashi *et al.*, J. Cell Biol., vol. 145(3):563-77 (1999)) ("Oohashi"). In particular, the Examiner has indicated that the Oohashi reference describes a protein that includes residues 750-850, 1250-1400 or 1490-1750 of SEQ ID NO:14.

Additionally, claim 5 and dependent claims 10, 12-14, 39, 42, 50-53 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Wang *et al.*, EMBO, vol. 17(13):3619-30 (1998)) ("Wang"). According to the Examiner, Wang describes proteins that comprise residues 1100-1200 of SEQ ID NO:14.

Finally, claim 5 and dependent claims 10, 12-14, 39, 42, 50-53 have been rejected under 35 U.S.C. § 102(a) as being anticipated by Nagase *et al.*, DNA Res., vol. 7(1):65-73 (2000)) ("Nagase"). In particular, the Examiner has indicated that the Nagase reference describes a protein that includes residues 1760,2300, 2400-2600 or 2650-2725 of SEQ ID NO:14.

As described above, the pending claims have been amended herein. In particular, independent claim 5 and its respective dependent claims (including claim 10, 12-14, 39, 42, and 50-53) have been amended to recite an isolated nucleic acid molecule comprising a nucleic acid

sequence encoding a polypeptide comprising an amino acid sequence selected from the group consisting of a mature form of the amino acid sequence SEQ ID NO:14 and SEQ ID NO:14.

In contrast to the nucleic acids of the claimed invention, the Schaefer, Oohashi, Wang and Nagase references do not disclose a nucleic acid encoding either a polypeptide of SEQ ID NO:14, the mature form of the polypeptide of SEQ ID NO:14 or a variant of the polypeptide of SEQ ID NO:14. As such, each of these references fails to disclose every element of the claimed invention. Accordingly, amended claims 5, 10, 12-14, 39, 42 and 50-53 are novel over these references, and this rejection should be withdrawn.

CONCLUSION

Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

Reg No 53097

Ivor R. Elrifi, Reg. No. 39,529
Attorney for Applicant
c/o MINTZ, LEVIN
Tel: (617) 542-6000
Fax: (617) 542-2241
Customer No. 55111

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